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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/867,612	06/02/1997	YI WANG	ALX-149	2350

7590 10/16/2002

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EXAMINER
GAMBEL, PHILLIP

ART UNIT	PAPER NUMBER
1644	42

DATE MAILED: 10/16/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 08/867,611	Applicant(s) WANG ET AL
	Examiner GAMBEL	Art Unit 1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 7/24/01.

2a)☑ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) _____ is/are pending in the application. 1-14, 17-34

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☑ Claim(s) _____ is/are rejected. 1-14, 17-34

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

1. Applicant's amendment, filed 7/24/02 (Paper No. 43), has been entered.

Claims 1-14 and 17-34 are pending and being acted upon presently

Claims 15 and 16 have been canceled previously.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action. This Office Action will be in response to applicant's arguments, filed 7/24/02 (Paper No. 43). The rejections of record can be found in previous Office Actions (Paper Nos. 21/31/34/38).

3. Yet once again, applicant should amend the first line of the specification to update the status of the priority application, which is now abandoned.

4. Again, the application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

"BALB/c" is the proper designation of this mouse strain. (e.g., see page 56, line 21 of the specification).

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate corrections are required

5. The amendment, filed 11/5/01 (Paper No. 37), stands objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

The amendments to pages 56 and 59-60 (see Appendices A, B, C and D) do not appear to have adequate written description in the application as-filed.

It does not appear that the specification provides for the adequate written description of "unique ability to bind to both alpha and beta chains of the human C5 protein in accordance with the teachings of Sims, et al. U.S. Patent No. 5,135,916" (see Appendices A and B).

Similarly, the written description of "two surprising properties" and "binds to both the alpha and beta chains of the human C5 protein" in the Appendices C and D do not appear to have written description in the specification as filed.

Applicant is required to review the underlined portions or newly added materials of the amendments to the specification set forth Appendices A-D and either cancel the new matter in the reply to this Office Action or provide sufficient direction to the written description for these amendments to the application as filed.

Applicant's arguments, filed 7/24/02 (Paper No. 43), have been fully considered but are not found convincing.

Applicant relies upon the entry of the above-mentioned amendment in USSN 08/236,208, which evolved into U.S. Patent No. 6,074,642, , wherein USSN 08/236,208 was incorporated by reference into the specification of the instant application in its entirety (see page 6, lines 6-7 and page 60, lines 11-16 of the instant specification).

Applicant is reminded that to incorporate material by reference, the host document must identify with detailed particularity what specific material it incorporates and clearly indicate where the material is found in the various documents. See Advanced Display Systems, Inc. v. Kent State Univ., 54 USPQ2d 1673 (Fed. Cir. 2000) citing In re Seversky, 177 USPQ 144, 146 (CCPA 1973).

In contrast, the reference to USSN 08/236,208 on pages 5-6, overlapping paragraph of the instant specification, is based on arthritis and not on a discussion of C5-specific antibodies, nor on the "unique ability to bind to both alpha and beta chains of the human C5 protein in accordance with the teachings of Sims, et al. U.S. Patent No. 5,135,916".

Further, page 60, paragraph 2 is a general statement of incorporating by reference in their entireties of the various publications and patent disclosures disclosed in the instant specification.

In neither disclosure relied upon applicant is there a specific identification with detailed particularity as to the specific materials introduced in the amendments to pages 56 and 59-60 indicated above.

The specification does not provide sufficient blazemarks nor direction for the above-mentioned amendments on page 56 and 59-60 of the instant specification. The instant specification now discloses limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action.

Applicant's arguments are not found persuasive.

6. Claims 19-34 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.

The specification as originally filed does not provide support for the invention as now claimed: "which binds the alpha chain of C5".

Applicant's amendment, filed 11/5/01 (Paper No. 37), directs support to the amendatory material to pages 56 and 59-60 of the specification, similarly filed 11/5/01 (Paper No. 37) (See Appendices A-D) for the written description for the above-mentioned "limitation".

Applicant's arguments, filed 7/24/02 (Paper No. 43), have been fully considered but are not found convincing essentially for the reasons above in Section 5.

Applicant's arguments and the examiner's rebuttal are essentially the same as addressed above.

The following of record is reiterated for applicant's convenience.

However, the disclosure of anti-C5 antibodies as C5 blockers does not provide sufficient written description for an antibody "which binds the alpha chain of C5".

In contrast, the instant claims appear to set forth a new subgenus by reciting However, the disclosure of anti-C5 antibodies as C5 blockers does not provide sufficient written description for an antibody "which binds the alpha chain of C5".

In contrast, the instant claims appear to set forth a new subgenus by reciting an antibody "which binds the alpha chain of C5", which, in turn, encompasses C5-specificities not disclosed in the specification as filed.

Applicant's reliance on generic disclosure and possibly a single species does not provide sufficient direction and guidance to the "claimed limitations" having the features currently claimed

It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. In re Smith 173 USPQ 679, 683 (CCPA 1972). See MPEP 2163.05(b).
Applicant's reliance on generic disclosure and possibly a single species does not provide sufficient direction and guidance to the "claimed limitations" having the features currently claimed

The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Applicant is claiming a subgenus not supported by the specification as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office action

Alternatively, applicant is invited to provide sufficient written support for the "limitation" indicated above.

Applicant's arguments are not found persuasive.

8.. Applicant's amendment, filed 11/5/01 (Paper No. 37), has provided the appropriate assurances for the deposit of the 5G1.1 antibody / hybridoma with respect to the deposit of biological materials under 35 USC 112, first paragraph.

9. Claims 1-17 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Sims et al. (U.S. Patent No. 5,635,178) for the reasons of record set forth in Paper No. 38.

Applicant's arguments, filed 7/24/02 (Paper No. 43), have been fully considered but are not found convincing essentially for the reasons of record set forth in Paper No. 38.

Applicant essentially asserts that Sims et al. is limited to teaching antibodies against P18, antibodies to C7 and antibodies to C9 and that Sims et al. does not teach antibodies specific for C5.

In contrast to applicant's assertions, Sims et al. claims methods and compositions comprising antibodies that specifically bind a component of the C5b-9 complex (see Claims 1-5). Given that C5b is a component of the C5b-9 complex, the claimed methods comprising antibodies that specifically bind a component of the C5b-9 complex reads on the claimed antibody specificity for C5.

In contrast to applicant's assertions, Sims et al. teach the treatment of patients with immune disorders and diseases such as rheumatoid arthritis (column 14, paragraph 2, particularly, line 28). Given the teaching of treating rheumatoid arthritis, Sims et al. Is teaching the treatment of a patient with established joint inflammation.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations encompassing properties of the active ingredient in the claims methods would be inherent properties of the claim methods to treat rheumatoid arthritis with antibodies that binds to a component forming the C5b-9 complex.

10. Claims 1-14, 17 and 19-33 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Sindelar et al. (U.S. Patent No. 5,173,499; 1449) AND/OR Sims et al. (U.S. Patent No. 5,635,178) in view of Auda et al. (Rheumatol. Int.10: 185-18, 1990; 1449) , Wurzner et al. (Complement Inflamm. 8: 328-340, 1991; 1449) and Montz et al. (Cell. Immunol. 127: 337-351, 1990; 1449) essentially for the reasons of record.

Claims 1-14, 17, 18 and claims 19-34 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Sindelar et al. (U.S. Patent No. 5,173,499; 1449) AND/OR Sims et al. (U.S. Patent No. 5,635,178) in view of Auda et al. (Rheumatol. Int.10: 185-18, 1990; 1449) , Wurzner et al. (Complement Inflamm. 8: 328-340, 1991; 1449) and Montz et al. (Cell. Immunol. 127: 337-351, 1990; 1449) as applied to claims 1-14, 17, 18 and 29-34 above and in further evidence of Rollins et al. (U.S. Patent No. 5853,722; of record) essentially for the reasons of record. for the reasons of record

Applicant's arguments, filed 7/24/02 (Paper No. 43), have been fully considered but are not found convincing essentially for the reasons of record set forth in Paper No. 38.

Applicant's arguments, in conjunction with the Wang declaration under 37 C.F.R. § 1.132, filed 3/25/99 (Paper No. 18), and the examiner's rebuttal are essentially the same as of record set forth in Paper No. 38.

Wang asserts that it was known at the time the invention was made that animals carrying a genetic defect such that they can produce no C5 can still established joint inflammation.

Further Wang asserts that while preliminary prophylaxis results showed a an unexpectedly dramatic effect in inhibiting the development of joint inflammation, he predicted that C5 blocker administration would not be effective in treating established joint inflammation in the absence of anti-T cell treatments for effective treatment.

Again, applicant argues that Sindelar et al. is directed to chemically synthesized non-protein organic compounds for the inhibition and/or suppression of immune activity and that Sindelar et al. does not disclose the use of antibodies.

While Sindelar et al. is directed to chemical compounds, Sindelar et al. clearly teach the biological effects of C5a ,including its role in arthritis (see Background of the Invention, including Tables II / III) and clearly teach administering inhibitive compounds which ameliorate or prevent detrimental effects caused by the complement system, including C5a for diseases or disorders such as those listed in Table III (e.g. see Therapeutic Uses of the Compounds of the Invention).

Again, applicant is reminded that Sims et al. (U.S. Patent No. 5,635,178) has been added to the rejection of record. Sims et al. teach methods of inhibiting platelet or endothelial cell activation by complement proteins comprising the administration of an antibody which specifically binds to a component forming the C5b-9 complex, including effective amounts to inhibit disorders such as arthritis (see entire document, including Claims 1-3).

As pointed out above and in contrast to applicant's assertions, Sims et al. claims methods and compositions comprising antibodies that specifically bind a component of the C5b-9 complex (see Claims 1-5). Given that C5b is a component of the C5b-9 complex, the claimed methods comprising antibodies that specifically bind a component of the C5b-9 complex reads on the claimed antibody specificity for C5. Alternatively, this teaching of targeting the C5b-9 provides for sufficient direction and motivation to target C5 with an expectation of success

Also, as pointed out above and in contrast to applicant's assertions, Sims et al. teach the treatment of patients with immune disorders and diseases such as rheumatoid arthritis (column 14, paragraph 2, particularly, line 28). Given the teaching of treating rheumatoid arthritis, Sims et al. is teaching the treatment of a patient with established joint inflammation.

Therefore, the prior art is directed towards inhibiting the same target (complement, C5 or C5a) and the same disorders or diseases (e.g. arthritis as it reads on established joint disease), encompassed by the claimed invention.

It is noted that Sims et al. teach targeting various diseases or disorders by inhibiting complement-mediated events, including arthritis and conditions such as vascular occlusion, reocclusion after surgery, coronary thrombosis and myocardial infarction, which are the subject of the methods taught by Rollins et al. Therefore, it was recognized by the ordinary artisan at the time the invention was made that inhibiting complement-mediated events, including C5- / C5a-mediated events, the ordinary artisan could inhibit various disorders and that targeting one disorder could provide an expectation of success in treating the other. For example, the teachings of Rollins et al., including its teaching of the 5G1.1. specificity on inhibiting complement /C5a activity in extracorporeal circulation could inhibit arthritis, as indicated by the teachings Sindelar et al. (e.g. see Table III) as well as Sims et al. (e.g. Claims 1-3)

Again, applicant argues that Wurzner et al. does not disclose the use C5-specific antibodies to treat joint inflammatory conditions. At best, applicant asserts that Wurzner only speculates that such anti-C5 antibodies may be useful to arrest the complement cascade, which may be beneficial for some diseases.

Applicant argues that Wurzner et al. teach C5b-specific antibodies and not C5a-specific antibodies.

With respect to the C5a specificity, Wurzner et al. clearly teach antibodies that inhibit the biological effects of C5a and TCC (see Discussion).

Again, applicant argues that Montz et al. is directed toward the role of anti-C5 antibodies in T cell proliferation in vitro and not to treating joint inflammation in a patient.

Again applicant asserts that Auda et al. description of elevated C5b-9 complex levels in patients with chronic rheumatic diseases is interesting, but refers to the mouse studies in which C5 was completely absent due to a genetic defect continued to develop established joint inflammation. Applicant further argues that Auda et al. do not suggest which of many complement component complexes would be the most effective, including the importance of the alpha chain of C5.

Again, applicant argues that Rollins et al. does not remedy the deficiencies of Sindelar et al., Auda et al., Wurzner et al. and Montz et al. Applicant asserts that Rollins et al. teach the use of anti-C5 antibodies to block the generation of activated complement components C5a and C5b following extracorporeal circulation during cardiopulmonary bypass, which is distinguished from the instant established joint inflammation.

Again, with respect to nonanalogous art, it has been held that the prior art reference must either be in the filed of applicant's endeavor or, if not then be reasonably pertinent to the particular problem with which the applicant was concerned in to order to be relied upon as a basis for rejection of the claimed invention. See In re Oetiker 24 USPQ2d 1443 (Fed. Cir. 1992).

In this case, the combination of prior art references are drawn to the inhibition of complement-mediated activity, including C5-mediated activity, and the inhibition of complement-mediated inflammatory processes, such as arthritis. See Sindelaar et al. and Sims et al.

Also, it appears that applicant's arguments addressed the references individually. One cannot show non - obviousness by attacking references individually where the rejections are based on combinations of references. In re Keller , 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc. , 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145.

Applicant's arguments are not found persuasive.

1. No claim is allowed.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

PHILLIP GAMBEL

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October 11, 2002